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Risk Assessment for Bees 2: Recent regulatory developments in North America

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Risk Assessment for Bees 2 – Recent regulatory developments in North America

Continuing on from our recent article *"Risk Assessment for Bees I – Recent Regulatory Developments in Europe"* this follow-up article focuses on developments in the area of pollinator regulatory testing and risk assessment in North America.

Since 1907, honeybees have been transported long distances in the US as a source of commercial pollination, initially by rail and from 1925 also by road. This has been an essential resource for farmers involved in large scale cultivation of a range of flowering crops including nuts (particularly almonds), and fruit crops. The increased use of 'mobile' honey bees for pollination led to the import of additional colonies from Australia in 2004 to meet pollination requirements of almond growers in California.

It had been noted that the numbers of commercial honey bee colonies had steadily been in decline since 1950 (six million) down to *ca*. three million in 1995. A report by the North American National Research Council - the National Academies stated "*...if the populations continue to decline at the rates exhibited from 1947 to 1972 and from 1989 to 1996, they would vanish by 2035.*" (1)

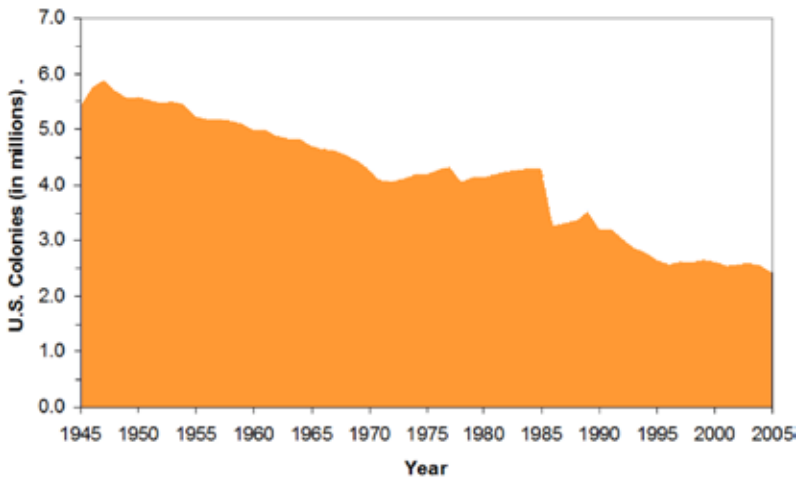
In response to this concern the North American Pollinator Protection Campaign was launched (18 October 2006). Ironically, this also coincided with the first reports of so called "Colony Collapse Disorder" (CCD) - first reported in October and December 2006, on the West Coast. CCD is characterised by sudden loss of a colony's worker bee population with very few dead bees being found near the colony; the queen, larvae and food left at the hive, with scavengers being slow to move in. This has resulted in a concerted effort between the US EPA, Canada's Pest Management Regulatory Agency (PMRA) and California's Department of Pesticide Regulation (CDPR) working together with a number of research institutes to investigate the causes and possible solutions.

At a conference in April 2007, fifty bee researchers convened at a workshop at USDA Beltsville Agricultural Centre (BARC), to prioritise CCD research objectives. The four most likely causes were identified as:

- Insecticides (particularly the neonicotinoids)
- Novel pathogen or parasite
- Immune suppression relating to management practices
- Decline in the nutritional adequacy of diet

These four areas could all be related to the gene families, which appear to be smaller in the honeybee genome, than in the genome of other insects. The full honey bee genome, which was reported in Nature in October 2006(2), confirmed the honey bee to have 10,157 genes, but with lower numbers of genes responsible for the areas of immunity and detoxification enzymes, which could render them more susceptible to infection and poisoning.

Figure 1: U.S. honey bee colonies, 1945-2005. Data compiled from USDA-NASS



Regulatory implications

Because of the potential link with crop protection products, the EPA has taken steps to provide additional guidance to their assessors in the Environmental Fate and Effects Division (EFED), to help them identify when it is appropriate to request additional data, and what data may be appropriate(3).

Until the issue of this guidance in October 2010, the requirements under Title 40 (Protection of the Environmental) of the Code of Federal Regulations (CFR) Part 158 (Data requirements for Pesticides) Subpart G (Ecological Effects) specified the following:

1 - Honey bee acute contact toxicity testing, where the result of this indicated a toxicity of less than 11 µg/bee, and the use patterns indicate the possibility of exposure conduct of a Tier 2 foliar residue toxicity test

2 - Field testing of pollinators would be considered necessary:

- where the residue toxicity study indicated extended residual toxicity
- data derived from other arthropod studies indicate potential chronic reproductive or behavioural effects
- data from other sources, e.g. university research or Experimental Use Permit program indicated potential adverse effects on colonies

These tests were required for the active substance. The Canadian Authorities also required the oral toxicity to be evaluated over 24 and 48 hours, and where there was evidence of increasing toxicity, the test could be extended to 96 hours.

The Interim Guidance suggested an approach closer to that currently adopted in the EU, and made reference to both OECD methods, and the OEPP/EPPO Bulletin articles providing both details of the test methods[4] and Risk assessment Scheme[5]. Both these documents were revised and reissued in September 2010, to reflect the current state of the science and knowledge including recommendations for the International Commission for Plant–Bee Relationships (ICPBR).

Whilst evaluating data submissions the reviewers will now be considering firstly the route of possible exposure:

- Direct contact
- Dermal/foliar residue
- Oral exposure (e.g. ingestion via pollen or nectar)

For each of these exposure routes they will then need to consider additional questions.

Direct contact exposure:

- The method of application: e.g. foliar spraying
- Attractiveness of the crop: is it a crop likely to be foraged by bees?
- Timing of application: does the time of application coincide with bloom?
- Toxicity: is the pesticide acutely contact toxic?

Dermal (foliar) residue exposure

- Contact toxicity: is the pesticide moderately to highly toxic on contact (i.e. LD_{50} < 11 µg/bee), and is there evidence of prolonged toxicity?
- Use pattern: Does the use pattern indicate possible contact as a result of foliar residue e.g. is the pesticide persistent?

From this the need for some form of label restriction to mitigate exposure and risk could be considered. If this is not possible higher tier testing, e.g. semi-field cage or tunnel tests should be considered.

Oral exposure

Exposure from pollen and nectar: what information is available to suggest exposure via this route? Consider the following:

- Is the pesticide systemic?
  - Consider use of metabolism magnitude of residue data
  - Consider physico-chemical data (Kow, and pKa)
  - Consider mode of application (e.g. seed treatment insecticide)
- Is the pesticide persistent?
  - Residues in nectar and pollen could result from application
  - Consider use of metabolism magnitude of residue data
- Are the crops attractive to bees?
  - Consider both target crops and rotational crops
- What data exists in the literature or other sources support possible exposure via pollen and nectar?

Based on these questions the need for additional data would be considered that would investigate the magnitude of exposure via pollen and nectar, e.g. field crop residue studies and semi-field cage or tunnel tests. In this case an oral acute toxicity test would also be required to interpret the data.

What information exists to suggest that the pesticide is toxic at environmentally relevant concentrations via the oral route of exposure? How likely is it that brood or other stages may differ in sensitivity from the adult worker tested in the contact test?

- Consider OECD oral toxicity test

- Does the mode of action suggest life stage related toxicity issues, e.g. insect growth regulators?
- Is there available information on the developing brood, e.g. OECD semi-field studies, or bee brood data?
- Consider evidence of sub-lethal effects which would relate to colony health but would not be captured by existing data.

From these questions consider requesting data demonstrating evaluation of toxicity via pollen or nectar, e.g. adult oral toxicity, *in-vitro* larval toxicity, bee-brood toxicity, semi-field tunnel or field studies.

In the absence of data, it was proposed other compounds with similar modes of action and/or similar structures could potentially be used for bridging purposes to characterise potential hazards.

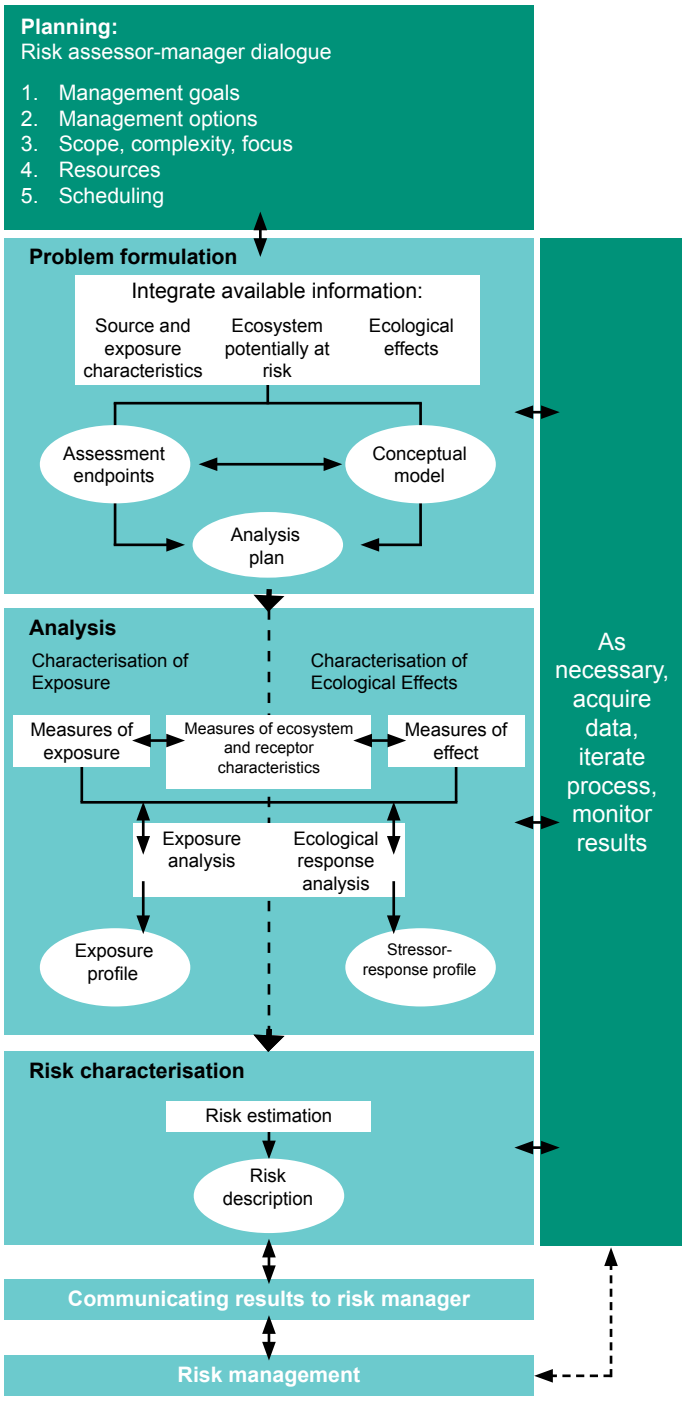
This interim guidance was expected to be superseded by recommendations expected to come from a SETAC (Society of Environmental Toxicology and Chemistry) Global Pellston Workshop on Pesticide Risk Assessment for Pollinators (January 2011). Whilst the final proceedings are still not yet available, a detailed summary is available for the SETAC web site[6]. The summary suggests that consideration of the impact on pollinators goes further to protect not only 'cultivated' honeybees but also non-*Apis* pollinators, with the following protection goals specified:

- Protection of pollination services provided by *Apis* and non-*Apis* species
- Protection of honey products and other hive products
- Protection of pollinator biodiversity; that is protection of adequate numbers and kinds of bee species that contributes to the health of the environment (primarily non-*Apis* bees)

This brings the US recommendations even closer to those now recommended in the EU in the recently published final EFSA guidance[7] (see page 10 for update), with testing not only of honeybees, but of non-*Apis* species, once suitable protocols are available, and inclusion of a chronic oral test with honey bee larvae as standard at Tier 1 for all compounds where larval exposure is possible. Until such time as non-*Apis* testing methods are available, they recommend the use of existing non-target arthropod data and bee data with a safety factor applied for evaluating the risk to non-*Apis* pollinators. In addition, not only the active substance, but also 'specific product formulations will require testing in certain cases' (unspecified in the summary). Higher tier testing in the form of semi-field cage or tunnel tests as well as full field trials are also advocated where there is a perceived risk. The ecological risk assessment process is summarised in Figure 2, and the proposed testing requirements for foliar applied products and those applied to soil or as seed treatments are summarised in Figures 3 and 4 respectively (shown on pages 8 and 9).

The meeting summary also recommends that in future ecological models may prove a useful tool in evaluating the risk to pollinators so that factors including adaptive behaviour, population structure, exposure patterns

Figure 2: Diagram of the interactive risk assessment process consisting of three phases i.e. problem formulation, analysis and risk characterisation. (As proposed at the SETAC Pellston Workshop and presented in the EPA White paper)



and landscape structure can be taken into account. This was identified as an important research topic, since whilst promising models are currently under development they require further work. A number of other important areas for research were also identified including:

- Development of an exposure nomogram for pesticide concentrations in pollen and nectar
- Evaluation of exposure data from trunk injection
- Potential for exposure through guttation
- Better understanding of pesticide fate within a colony
- Modification and validation of larval feeding test
- Development of a standardised protocol for a chronic feeding study
- Development of a method to assess effects on foraging behaviour
- Development of an artificial diet for use in larval testing
- Toxicity testing for non-*Apis* species
- Improved methods of monitoring of effects in the field

In August 2012, the US EPA released a document entitled "White Paper in Support of the Proposed Risk Assessment Process for Bees". The White Paper, a comprehensive 275-page document, was the result of collective efforts by the EPA, the Pest Management Regulatory Agency of Canada and the California Department of Pesticide Regulation[8]. It was reviewed at a meeting of the FIFRA Scientific Advisory Panel (SAP) in September 2012. The minutes of the meeting (102 pages) were released in December 2012[9].

The white paper appears to support and build on the recommendations of the SETAC meeting. In particular it makes reference to different methods to estimate pesticide concentrations in pollen and nectar for pesticide applications made via foliar spray, soil treatment, seed treatment and tree trunk applications. This was identified at the SETAC workshop as an important future research topic. In screening-level assessments, contact exposure is estimated for pesticides applied via foliar spray. An upper residue value of chemicals on honey bees based on Koch and Weisser 1997[10] is proposed to represent contact exposures. The estimation of dietary exposure to pesticides applied via foliar spray, soil treatment, or seed treatment, involves a few different methods. For foliar spray applications, the proposed approach involves the use of the tall grass residue value from the T-REX model (v. 1.5) as a surrogate for pesticide concentrations in nectar and pollen. This has been validated using measured concentrations in nectar for eight different pesticides from seven studies. For soil treatments, the proposed Tier I method for estimating exposure involves the use of the Briggs' soil-plant uptake model, which is designed to estimate pesticide concentrations in plant shoots; these estimated concentrations in plant shoots are used as a surrogate for concentrations in pollen and nectar. For seed treatments, the proposed Tier I exposure method is based on the ICPBR 1 mg a.i./kg concentration as an upper-level for pesticides in nectar and pollen.

Conclusions

In both the EU and North America the requirements for honey bee regulatory testing have increased significantly in response to the heightened awareness of declining pollinator numbers. For registrants submitting in the EU the revised US recommendations are unlikely to result in additional testing. However, for re-registrations or review in the US further consideration of the adequacy of existing data is likely to be required.

The global nature of the concern for our pollinators has resulted in a rarely seen co-operation and level of discussion which for once has resulted in new regulatory schemes which are relatively consistent on both sides of the Atlantic. Time will tell if they prove to be appropriate.

References

1 National Research Council of the National Academies; Status of pollinators in North America. October 2006

2 The honeybee Genome Sequencing Consortium; Insights into social insects from the genome of the honeybee Apis mellifera. Nature Vol 443, October 2006 pp 91-949.

3 United States Environmental Protection Agency Memorandum, October 19, 2011: Interim Guidance on Honey bee Data Requirements

4 European and Mediterranean Plant Protection Organization: Efficacy Evaluation of Plant Protection Products. Side effects on honeybees. Revised September 2010. (PP 1/170(4)). 2010 OEPP/EPPO Bulletin 40 pp 313-319.

5 European and Mediterranean Plant Protection Organization: Environmental Risk Assessment Scheme for Plant Protection Products. Chapter 10 Honeybees. Revised September 2010. (PP 3/10(3)). 2010 OEPP/EPPO Bulletin 40 pp 23-331.

6 Fischer, D., Moriarty T. 2011. Pesticide risk assessment for pollinators. Summary of a SETAC Pellston Workshop, Pensacola FL. (USA): Society of Environmental Toxicology and Chemistry (SETAC)

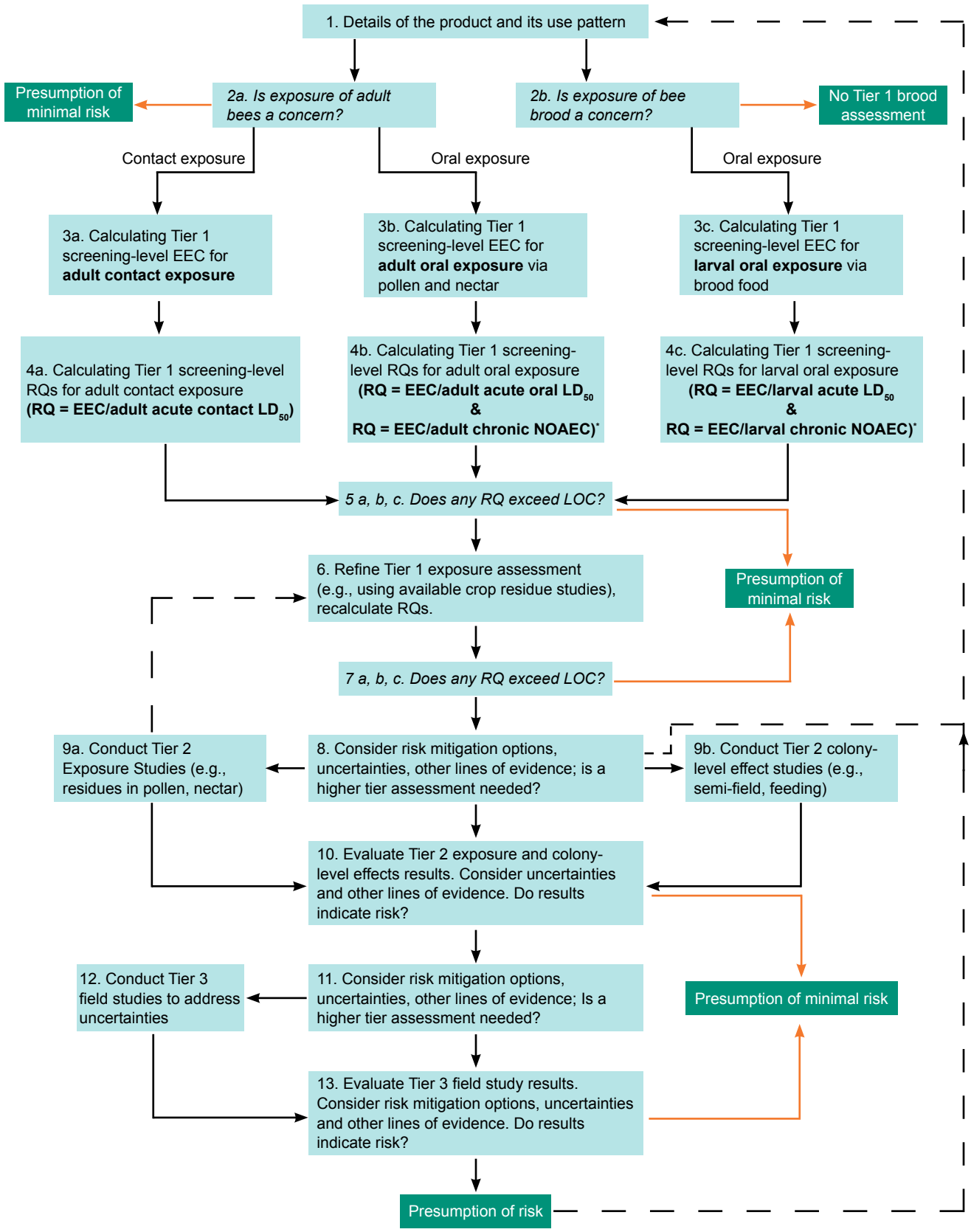
7 European Food Safety Authority, 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus* spp. and solitary bees)

8 http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004

9 Public Docket EPA-HQ-OPP-2012-0543, http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2012-0543;dct=FR+PR+N+O+SR

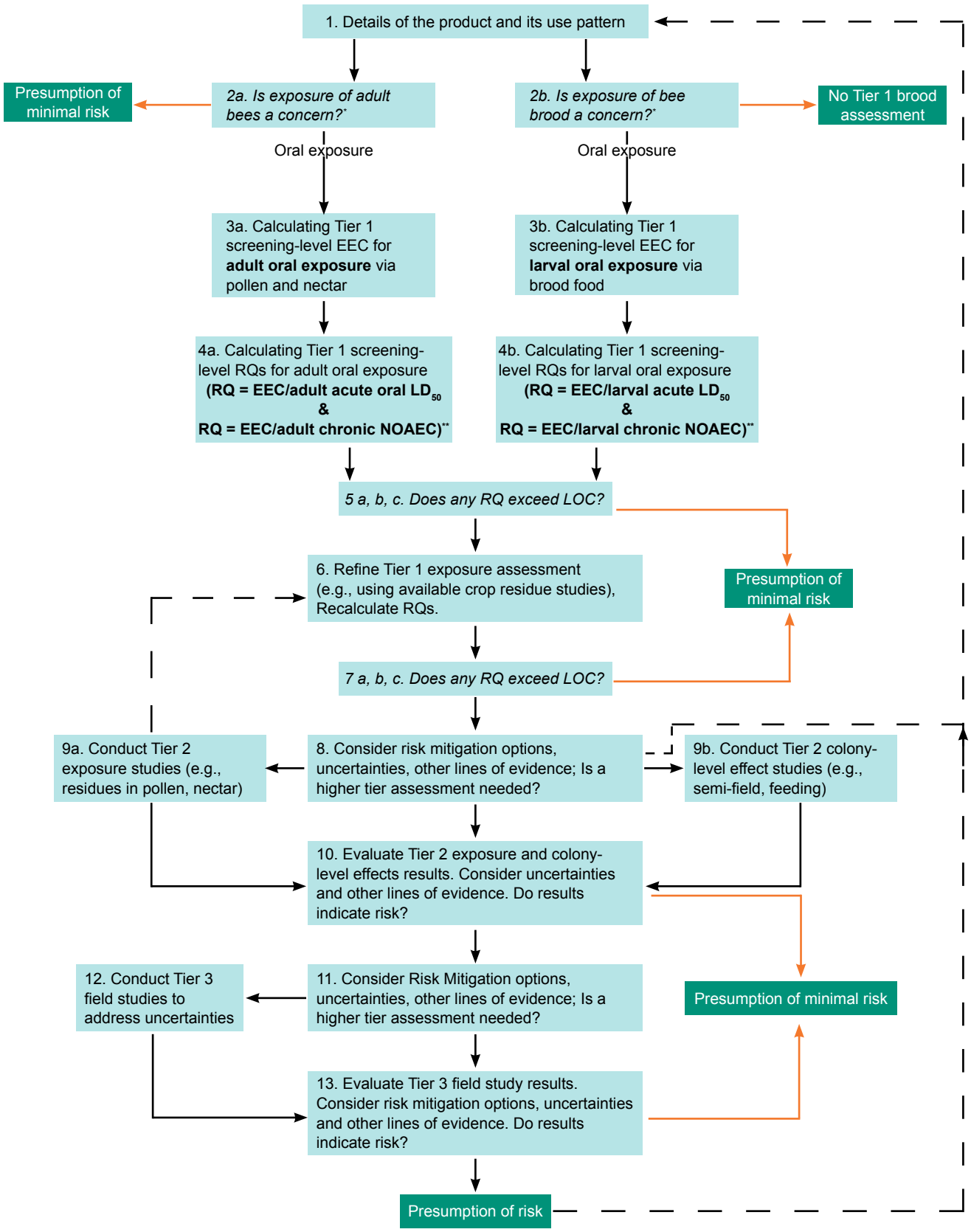
10 Koch, H. and P. Weisser. 1997. Exposure of honey bees during pesticide application under field conditions. Apidologie, 28: 439-447.

Figure 3: Proposed Tiered Approach for assessing risk to honeybees from foliar spray applications (As proposed at the SETAC Pellston Workshop and presented in the EPA White paper)



*When tests are sufficiently developed and validated

Figure 4: Proposed Tiered testing approach for assessing risk to honeybees from soil or seed treatments (As proposed at the SETAC Pellston Workshop and presented in the EPA White paper)



*Mitigation of risks from abraded seed coating are addressed outside of this process

**When tests are sufficiently developed and validated

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